Implications of COVID-19 for an ageing population

An evolving public health policy in response to the COVID-19 pandemic must address the needs of older people

Coronavirus disease 2019 (COVID-19) encompasses a broad clinical spectrum caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Accumulating evidence indicates a strong age-related gradient for risk of severe disease, hospitalisation and death. A model-based analysis found that hospitalisation estimates for COVID-19 increased with age: 1.04% for people aged 20–29 years, increasing to 18.40% for those aged 80 years and older.[1] Applying these infection fatality rates (assuming a uniform attack rate by age group) to the Australian population,[2] we project that if 0.5 million Australians were infected with SARS-CoV-2, 66% of deaths would occur in those aged 70 years and older. Eighty-eight percent of deaths would occur in Australians aged 60 years and older (Box 1).

The individual contributions related to frailty and physiological changes associated with ageing or multimorbidity remain uncertain. Given Australia's ageing population (21.4% are aged 60 years and older),[2] an evolving public health policy in response to the COVID-19 pandemic must address the needs of this vulnerable population. Key points regarding COVID-19 infection in older people are summarised in Box 2.

Specific populations

Health care workers account for an estimated 20% of positive cases in Italy,[3] 14% in the United Kingdom,[4] and 11% in the United States.[5] In Australia in 2018, the average age of practising general practitioners and specialists was 51.1 and 49.9 years, respectively.[6] This creates complex challenges to strained health infrastructure and resources to ensure allocation of vulnerable staff to non-COVID-19-related roles while maintaining valuable clinical experience. Evidence for risk stratification for health care workers is currently lacking; specific occupational risk of SARS-CoV-2 infection and individual risk of morbidity and mortality (eg, age, medical comorbidities) must be assessed on a case-by-case basis.

Residents of long term care facilities are generally older, multimorbid, and restricted in their capacity to self-isolate. The World Health Organization has estimated that up to half of COVID-19-related deaths in Europe were residents of long term care facilities.[7] As of 1 September 2020, 462 of the 657 deaths in Australia had occurred in aged care services. The median age for all deaths is 86 years.[8] Importantly, of the 48 residents of one American residential facility who tested positive for SARS-CoV-2, 27 (56%) were asymptomatic at the time of testing.[9] This highlights that infection control measures targeting symptomatic patients only are inadequate.

Another important consideration is community dwelling older people with cognitive impairment and an inability to comprehend social distancing recommendations, including the ability to report symptoms or recent contacts.

Resources for facilities and health care workers are available to guide management (Supporting Information, Box 1).

Impact of medical comorbidities

Comorbidities associated with more severe disease include hypertension, cardiovascular disease, diabetes, obesity and malignancy. A review of 5700 patients hospitalised in the New York area with COVID-19 (median age, 63; interquartile range, 52–75 years), the most prevalent comorbidities were hypertension, obesity and diabetes (56.6%, 41.7% and 33.8%, respectively).[10]

Importantly, associations for individual comorbid conditions have not been established in either

Nicolette R Holt[1,2]

Johannes T Neumann[3,4]

John J McNeil[3]

Allen C Cheng[3]

1 Royal Melbourne Hospital, Melbourne, VIC.
2 Peter MacCallum Cancer Centre, Melbourne, VIC.
3 Monash University, Melbourne, VIC.
4 University Heart and Vascular Center, Hamburg University of Applied Sciences, Hamburg, Germany.

Nicolette.Holt@mh.org.au

1 Projected Australian deaths if 0.5 million SARS-CoV-2 infections occur, by age group

Age group	Proportion of total population*	Infection fatality rate[†]	Number of deaths if 0.5 million infected	Proportion of deaths
0–9 years	12.56%	0.002%	1	< 1%
10–19 years	12.05%	0.007%	4	<1%
20–29 years	14.45%	0.031%	22	<1%
30–39 years	14.48%	0·084%	61	1%
40– 49 years	12.91%	0.161%	104	2%
50–59 years	12.14%	0.595%	361	8%
60–69 years	10.30%	1.930%	994	28%
70–79 years	7.06%	4.280%	1511	33%
≥ 80 years	4.02%	7.800%	1568	34%

* Australian population data from Australian Bureau of Statistics.[2] † Infection fatality rates from Verity et al.[1] ◆

> **2 COVID-19 in older people: key points**
>
> - COVID-19 encompasses a broad spectrum of clinical presentation and disease severity. Globally, case fatality rates demonstrate a strong age-related gradient.
> - Baseline medical comorbidities associated with severe disease and death include hypertension, cardiovascular disease and diabetes. Importantly, causative associations for individual comorbid conditions have not been established.
> - Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and non-steroidal anti-inflammatory drugs should continue to be prescribed according to current guidelines.
> - Unintended consequences of non-COVID-19-related medical issues include a trend to delayed presentation and management of other acute medical issues, and the sequel of elective surgery postponement.
> - Health policies of social distancing and visitor restriction in residential aged care facilities also increase psychological distress in susceptible individuals. Adaptive models of care (eg, telehealth consultations) can facilitate ongoing management of regular comorbidities.
> - Because of immunosenescence, a SARS-CoV-2 vaccine may not translate into lasting immunity in an older population. The indiscriminate use of non-validated therapies to treat COVID-19, such as hydroxychloroquine and azithromycin, should be discouraged in older people due to increased risks of adverse effects (eg, QT-interval prolongation, ventricular tachyarrhythmia and sudden cardiac death).
> - Asymptomatic transmission remains a constant threat to older people and has implications for infection control measures; community surveillance must go beyond targeting only symptomatic individuals.

predisposing to SARS-CoV-2 infection or disease severity and mortality. Furthermore, in many studies, baseline characteristics in patients with COVID-19 were not adjusted for potential confounders such as age.

It is too early to comprehensively evaluate lasting morbidity in COVID-19 survivors. Given the increased risk of hospitalisation and morbidity among older people, a key focus of any public health strategy must be on implementing systems for the long term surveillance and management of those who recover from the acute effects of COVID-19 only to face lasting disabilities into the future.

Uncertainty regarding use of regular medications

Angiotensin-converting enzyme 2 (ACE2), an enzyme that counters renin–angiotensin–aldosterone system (RAAS) activation, is co-opted by SARS-CoV-2 to gain entry into human epithelial cells.[11] ACE2 is expressed in multiple organs, including heart, kidney and respiratory alveolar epithelium, the primary target of SARS-CoV-2.[12] There are conflicting theoretical concerns as to whether treatment with RAAS inhibitors, primarily ACE inhibitors and angiotensin receptor blockers (ARBs), could lead to altered ACE2 activity and levels, enhanced binding and entry of SARS-CoV-2 into respiratory epithelial cells, or increased disease severity in patients with confirmed COVID-19.[13] A contrasting theory is that increased ACE2 activity could be degrading angiotensin II and may lead to beneficial effects.

Currently, clinical data and experimental evidence are lacking regarding either adverse or beneficial outcomes from continued use of ACE inhibitors and ARBs in the setting of COVID-19.[13] Given the well established benefits in cardiovascular disease, and that indiscriminate discontinuation may lead to decompensation and hospitalisation, relevant professional organisations have recommended continuation of regular RAAS antagonists in the absence of proven risk (Supporting Information, Box 2). Further prospective epidemiological clinical trials are required to inform the safety of continuing ACE inhibitors and ARBs in patients with COVID-19.

Concerns about the use of non-steroidal anti-inflammatory drugs (NSAIDs) in treating COVID-19 were based on case reports only.[14] Given the current lack of clinical studies to evaluate risk, NSAIDs should not be discontinued. Similarly, initiation of NSAIDs in the absence of contraindications does not need to be avoided in patients with COVID-19.

Unintended consequences: non-COVID-19-related medical issues

A secondary consequence to emerge from the COVID-19 pandemic is the alterations in delivery of usual standards of care for non-COVID-19-related medical issues, including primary care and preventive medicine (eg, cancer screening).

A trend towards delayed presentation and management of acute medical issues, including acute coronary syndromes and strokes, has been noted. Despite timely reperfusion being standard of care for ST-segment elevation myocardial infarction (STEMI), there has been an observed reduction in cardiac catheterisation laboratory STEMI activations in America by 38%[15] and in Spain by 40 %.[16] Similar observations are occurring for stroke.[17] The delay in presentation, if patients present at all, for these time-critical issues is considered secondary to fear of contracting COVID-19 from hospitalisation.

Digital revolution for health care delivery

Adaptive models of health care delivery, such as telehealth consultations, have rapidly been adopted to ensure ongoing delivery of essential health care services.[18] Facilitating transition to digital health care delivery for both community and residential patients will face challenges in an ageing population for multiple reasons, including technology literacy and infrastructure restrictions. This was highlighted in a US-based study of 4525 adults aged over 65 years which found that 35% of participants experienced telemedicine unreadiness.[19]

The restrictions associated with telehealth in older people are amplified in the management of pre-existing psychiatric or neurocognitive disorders; globally, more than 50 million people have dementia.[20]

Although Australia has been well positioned to rapidly expand established telehealth services,[21] the reach of uptake and therapeutic success of telehealth in older people in addressing issues of cognitive and mental health disorders remains uncertain.[22] Quality of outcomes, both positive and negative, from these adaptive models of health care service delivery requires ongoing evaluation.

Psychological impact of isolation

Older people are more susceptible to social disconnection and isolation, leading to increased symptoms of anxiety and depression.[23] A review of quarantine measures for COVID-19 identified quarantine duration, inadequate supplies, financial concerns and infection fears as some of the key triggers for psychological distress.[24] The loss of direct connection with routine health care providers from inability to have in-person interactions will also intensify distress and anxiety.

Unaddressed psychological and emotional distress has also shown in prior pandemics to reduce compliance with social distancing measures.[25] An effective COVID-19 public health response must incorporate a campaign of education and awareness, risk assessment and evidence-based interventions to address evolving mental health concerns, with a particular focus on people living with dementia and their caregivers.

COVID-19 and immunity

Longitudinal serological prevalence measurements are urgently required to establish extent and duration of immunity to SARS-CoV-2 infection. This has implications in evaluating the potential of herd immunity. Based on an estimated basic reproduction number for SARS-CoV-2 of 2.2,[26] 60% of the population would need protective immunity to mitigate against future substantial COVID-19 outbreaks.[27]

A large population-based study in Iceland suggested stability of SARS-CoV-2 humoral immunity up to 4 months after diagnosis.[28] The extent of protective antiviral immunity from antibodies to SARS-CoV-2 remains uncertain, as does the possibility of reinfection and the nature and degree of immunity required to protect against reinfection. Estimates from related coronaviruses suggest immunity was present after 1 year.[29]

Interruption of the global COVID-19 pandemic will likely rely on the development of an effective vaccine. The influenza vaccine is regarded as best practice for influenza prevention in older people. While more than 100 candidate SARS-CoV-2 vaccines are in development, the most ambitious estimates are 6–12 months until efficacy results from a phase 3 expansion trial are known.[30] There are also efforts by the World Health Organization to centralise vaccine development to ensure that immunological responses to various vaccines are uniformly measured. Importantly, activation of the immune system, in response to either wild-type infection or vaccination, may not translate into lasting immunity in older people owing to immunosenescence, the gradual deterioration of immunological response with age.[31] However, older people should be prioritised in receiving a SARS-CoV-2 vaccine.

Risks of unproven medication

Established evidence-based treatment for COVID-19 is currently lacking. Drugs proposed for management of COVID-19 include the antimalarial drugs (chloroquine and hydroxychloroquine), antivirals (lopinavir, ritonavir and remdesivir), interferon-β, and the interleukin-6 pathway inhibitor tocilizumab.

Preliminary evidence from randomised trials of hospitalised COVID-19 patients indicates a mortality benefit of low dose dexamethasone in patients requiring respiratory support,[32] and an accelerated recovery time with remdesivir in patients with pulmonary involvement.[33] Hydroxychloroquine, however, has not demonstrated a mortality benefit.[34] Evidence for the role of convalescent plasma in reducing the duration and severity of SARS-CoV-2 infection is still evolving.[35]

It is important to be mindful of the well established adverse side effects of these medications. Hydroxychloroquine and azithromycin independently increase risk of adverse cardiac events (eg, QT-interval prolongation, ventricular tachyarrhythmia and sudden cardiac death). Older people are more predisposed to adverse effects of these medications. Overall, the indiscriminate use of non-validated therapies to treat COVID-19 should be discouraged in older people outside registered clinical trials.

Conclusion: projecting the course of the pandemic

The projected course of the COVID-19 pandemic remains uncertain. In just over 7 months, SARS-CoV-2 has infected in excess of 25 million of the world's population, of which 508 055 (3.4%) have died.[36] Case fatality rates have demonstrated a strong age-related gradient. Australians aged over 65 years and those with comorbidities remain disproportionately vulnerable to hospitalisation and death. They are also at heightened risk of psychological distress from prolonged social distancing measures and the transition from trusted in-person health care delivery to digital platforms. Psychological health strategies must form an integral part of any COVID-19 public health response.

Results of prospective clinical trials are desperately needed to guide continuation of common prescription medications (eg, ACE inhibitors and ARBs), establish efficacy of chemoprophylaxis or pharmacotherapy options, and SARS-CoV-2 vaccine development, mindful of immunosenescence in older people.

With the COVID-19 risk projected to remain a public health concern, both locally and globally, for many months to come, strategies addressing the asymptomatic transmission of SARS-CoV-2 in the community are required. The ageing population remains especially vulnerable to bearing the burden of substantial morbidity and mortality.

References are available online.

Supporting Information

Additional Supporting information is included with the online version of this article.

1 Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis* 2020; 20: 669–677.

2 Australian Bureau of Statistics. 31010.0 Australian demographic statistics, Sep 2019. Canberra: ABS, 2020. https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3101.0Sep%202019?OpenDocument (viewed Apr 2020).

3 Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *Lancet* 2020; 395: 1225–1228.

4 Hunter E, Price DA, Murphy E, et al. First experience of COVID-19 screening of health-care workers in England. *Lancet* 2020; 395: e77–e78.

5 CDC COVID-19 Response Team. Characteristics of health care personnel with COVID-19 – United States February 12–April 9, 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69: 477–481.

6 Australian Government Department of Health. Health workforce data. https://hwd.health.gov.au/summary.html#part-1 (viewed Apr 2020).

7 World Health Organization. Preventing and managing COVID-19 across long-term care services: policy brief. GenevaWHO, 2020. https://www.who.int/publications/i/item/WHO-2019-nCoV-Policy_Brief-Long-term_Care-2020.1 (viewed Sept 2020).

8 Australian Government Department of Health. Coronavirus (COVID-19) at a glance. https://www.health.gov.au/resources/publications/coronavirus-covid-19-at-a-glance (viewed Sept 2020).

9 Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N Engl J Med* 2020; 382: 2081–2090.

10 Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020; 323: 2052–2059.

11 Li W, Moore MJ, Vasilieva N, Sui J, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature* 2003; 426: 450–454.

12 Hamming I, Timens W, Bulthuis ML, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol* 2004; 203: 631–637.

13 Vaduganathan M, Vardeny O, Michel T, et al. Renin–angiotensin–aldosterone system inhibitors in patients with Covid-19. *N Engl J Med* 2020; 382: 1653–1659.

14 Little P. Non-steroidal anti-inflammatory drugs and covid-19. *BMJ* 2020; 368: m1185.

15 Garcia S, Albaghdadi MS, Meraj PM, et al. Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. *J Am Coll Cardiol* 2020; 75: 2871–2872.

16 Rodríguez-Leor O, Cid-Álvarez B, Ojeda S, et al. Impact of the COVID-19 pandemic on interventional cardiology activity in Spain. *REC Interv Cardiol* 2020; 2: 82–89.

17 Sheth K. Hospital admissions for strokes appear to have plummeted ads, a possible sign people are afraid to seek critical help. *Washington Post* 2020; 9 Apr. https://www.washingtonpost.com/national/health-science/hospital-admissions-for-strokes-appear-to-have-plummeted-a-doctors-says-a-possible-sign-people-are-afraid-to-seek-critical-help/2020/04/08/2048b886-79ac-11ea-b6ff-597f170df8f8_story.html (viewed Aug 2020).

18 Keesara S, Jonas A, Schulman K. Covid-19 and health care's digital revolution. *N Engl J Med* 2020; 382: e82.

19 Lam K, Lu AD, Shi Y, Covinsky KE. Assessing telemedicine unreadiness among older adults in the United States during the COVID-19 pandemic. *JAMA Intern Med* 2020; https://doi.org/10.1001/jamainternmed.2020.2671 [Epub ahead of print].

20 Alzheimer's Disease International. World Alzheimer report 2019: attitudes to dementia. LondonADI, 2019.

21 Fisk M, Livingstone A, Pit SW. Telehealth in the context of COVID-19: changing perspectives in Australia, the United Kingdom, and the United States. *J Med Internet Res* 2020; 22: e19264.

22 Moreno C, Wykes T, Galderisi S, et al. How mental health care should change as a consequence of the COVID-19 pandemic. *Lancet Psychiatry* 2020; 7: 813–824.

23 Santini ZI, Jose PE, York Cornwell E, et al. Social disconnectedness, perceived isolation, and symptoms of depression and anxiety among older Americans (NSHAP): a longitudinal mediation analysis. *Lancet Public Health* 2020; 5: e62–e70.

24 Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet* 2020; 395: 912–20.

25 Manuell ME, Cukor J. Mother Nature versus human nature: public compliance with evacuation and quarantine. *Disasters* 2011; 35: 417–442.

26 Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020; 382: 1199–1207.

27 Guerra FM, Bolotin S, Lim G, et al. The basic reproduction number (R_0) of measles: a systematic review. *Lancet Infect Dis* 2017; 17: e420–e428.

28 Gudbjartsson DF, Norddahl GL, Melsted P, et al. Humoral immune response to SARS-CoV-2 in Iceland. *N Engl J Med* 2020; https://doi.org/10.1056/NEJMoa2026116 [Epub ahead of print].

29 Choe PG, Perera R, Park WB, et al. MERS-CoV antibody responses 1 year after symptom onset, South Korea, 2015. *Emerg Infect Dis* 2017; 23: 1079–1084.

30 World Health Organization. Draft landscape of COVID-19 candidate vaccines – 28 August 2020. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines (viewed Sept 2020).

31 Del Giudice G, Goronzy JJ, Grubeck-Loebenstein B, et al. Fighting against a protean enemy: immunosenescence, vaccines, and healthy aging. *NPJ Aging Mech Dis* 2018; 4: 1.

32 RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 – preliminary report. *N Engl J Med* 2020; https://doi.org/10.1056/NEJMoa2021436 [Epub ahead of print].

33 Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 – preliminary report. *N Engl J Med* 2020; https://doi.org/10.1056/NEJMoa2007764 [Epub ahead of print].

34 University of Oxford News Office. No clinical benefit from use of hydroxychloroquine in hospitalised patients with COVID-19. 5 June 2020. https://www.ox.ac.uk/news/2020-06-05-no-clinical-benefit-use-hydroxychloroquine-hospitalised-patients-covid-19-0 (viewed Aug 2020).

35 Piechotta V, Chai KL, Valk SJ, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. *Cochrane Database Syst Rev* 2020; (7): CD013600.

36 World Health Organization. WHO coronavirus disease (COVID-19) dashboard. https://covid19.who.int/ (viewed Aug 2020). ■